REMARKS

Upon entry of the foregoing amendments, claims 1, 6-13 and 15-27 will be pending in the application. Claims 1, 26 and 27 are the only pending independent claims. The Examiner withdrew claims 24-35 from consideration, since these were the claims that were not provisionally elected, with traverse. Non-elected claims 24-27 have not been canceled, and have been amended in the anticipation that they will be rejoined upon the indication of an allowable claim directed to the composition.

Amendment of the Specification

The specification has been amended to include section headings as required by the Examiner, though most are indicated as being "Not Applicable." The Brief Description of the Drawing section with the indicated drawing description has been moved to the appropriate location in the specification.

Reconsideration and withdrawal of the objections to the specification are respectfully requested.

Amendment of the Claims

Independent claims 1, 26 and 27 have been amended to specify that the claimed composition is in the form of an aqueous solution or suspension as set forth in original claim 2.

The independent claims also have been amended to recite that the claimed composition is in a form for nasal or ocular delivery. This is a selection from the list that appeared in original claims 24 and 29. Although original claims 24 and 29 included both ocular and ophthalmic delivery, since there is no difference between ocular and ophthalmic delivery, ophthalmic delivery has been deleted without affecting the scope of ocular delivery.

The independent claims additionally have been amended to indicate that the therapeutic agent is a systemically acting agent, as noted in original claims 31 and 35.

Also, the independent claims have been amended to indicate the nature of the derivative of chitosan, as set forth in original claim 9.

In view of the foregoing claim amendments, the original or preliminarily amended claims or the portions thereof that have been incorporated into the independent claims now have been canceled, without prejudice, or the incorporated portions have been deleted, without prejudice, to avoid redundant claiming.

The clauses regarding the salt, the derivative and the salt of the derivative in all claims reciting them have been clarified merely to make the language more efficient in view of the antecedent bases of the various terms used in these clauses, without narrowing the meaning of the claims.

The dependency of claim 11 has been changed so that claim 11 now depends from claim 10 instead of claim 12, based on the undersigned attorney's understanding of Applicants' intention that was not noticed during previous reviews of the claims.

Withdrawn claims 26 and 27 have been amended to place the claims, initially claiming a "use" in accordance with European patent practice, into process of treatment format consistent with U.S. patent practice. Use claims that would have been redundant if rewritten in accordance with U.S. patent practice have been canceled, without prejudice.

Since all of the foregoing amendments are supported by the application as filed and no new matter has been added, entry of the foregoing amendments is respectfully requested.

The Problem Addressed by the Invention

Although this application was originally written with a focus on the ability of the claimed compositions to gel on a mucosal surface, Applicants no longer wish to focus on this property. The key inventive concept as far as Applicants are concerned is to provide compositions for delivery of systemically acting therapeutic agents to a mucosal surface, where such compositions comprise chitosan or the claimed derivatives, salts and salts of derivatives of chitosan, along with a polyol-phosphate or sugar-phosphate salt and a plasticizer, for effective delivery of the therapeutic agent nasally or ocularly.

Obviousness

The Examiner considered that the compositions as previously claimed would have been obvious in view of the disclosure of Chenite *et al.* U.S. Patent 6,344,488 ("Chenite") and Dunn *et al.* U.S. Patent 5,702,716 ("Dunn"). Neither of these documents are particularly relevant to the compositions as now claimed.

Chenite describes temperature-controlled pH-dependent formation of ionic polysaccharide gels, such as chitosan/organo-phosphate aqueous systems.

The gels described in Chenite comprise 0.1 to 5% by weight of chitosan or a chitosan derivative; and 1.0 to 20% by weight of a salt of a polyol or sugar selected from the group consisting of mono-phosphate dibasic salts, mono-phosphate salts and a mono-carboxylic acid salts of polyol or sugar. The gel is induced and stable within a temperature range of 20 to 70°C and is adapted to be formed and/or gellated *in situ* within a tissue, an organ or cavities of an animal or a human. There is no disclosure or suggestion of the inclusion of a plasticizer in the compositions described in Chenite.

The compositions as now claimed are formulated for nasal or ocular delivery. Compositions suitable for delivery in this manner must have a particular set of properties which allow them to be successfully delivered to the nose or the eye. For example, they must have a viscosity which enables them to be sprayed or to be delivered in the form of drops. The gels described in Chenite are not intended for nasal or ocular delivery. As described at column 4, lines 61 to 67, Chenite's gels are used as or in implants for repair, reconstruction and/or replacement of tissues and/or organs for animals or humans or as transdermal or dermatological drug delivery systems. There is no disclosure or suggestion of the use of Chenite's compositions for delivery of a systemically acting therapeutic agent across the mucosal surface via nasal or ocular delivery.

It is clear from the discussion in Chenite at the top of column 5, and in the first full paragraph of column 13, for example, that the gels described are intended to provide a local effect, *i.e.* local treatment at the site of application. They are not intended to provide delivery of a systemically acting therapeutic agent across a mucosal surface.

In summary, there is nothing in Chenite to suggest that a composition as now claimed

could be used to successfully deliver a systemically acting drug through nasal or ocular delivery to a mucosal surface. The claimed invention would not have been obvious in view of the disclosure of Chenite.

Dunn describes a polymer system that can provide controlled release of bioactive agents from a matrix. Dunn also describes a liquid composition which comprises an organic solvent, a biocompatible, biodegradable thermoplastic polymer, a rate modifying agent and bioactive materials. The first thing to note is that the compositions of Dunn are not aqueous. Rather, they comprise an organic solvent. There is nothing in Dunn that would have encouraged the skilled person to replace this essential element of the compositions of Dunn with an aqueous solvent or that an aqueous solvent would even be compatible or effective in Dunn's composition. In fact, the teaching of Dunn discourages this. At column 6, lines 4 to 6, it is stated: "By necessity, the solvent system must be miscible with both the thermoplastic polymer and water." The skilled person in the art reading Dunn and particularly this portion, would have appreciated that an aqueous solvent system would not be compatible with the thermoplastic polymer and would not have even considered replacing the solvent system used in Dunn with an aqueous solvent system.

A polymer system which is a microporous solid matrix of the biocompatible, biodegradable thermoplastic polymer, the rate modifying agent and the bioactive material, is formed when the liquid composition of Dunn is applied to an aqueous medium that is internal or external to the body. The polymer system is substantially insoluble in aqueous media (see column 2, lines 18 to 41).

Liquids that form polymer systems of this type are completely unsuitable for the delivery of therapeutic agents via the nose or the eye. Compositions, such as those of the present invention, that deliver systemically acting therapeutic agents through the nose or the eye need to be retained at the mucosal surface of the nose or the eye for long enough for the therapeutic agent to be absorbed through the mucosal surface. After that time, the composition must be expelled from the nose or the eye. The polymer system of Dunn does not behave in this manner, as these polymer systems are intended to be retained at the site of application and to provide controlled release of a bioactive material.

It is also worth noting that it is not practical to provide sustained release via nasal or ocular delivery, as a composition delivered using these delivery routes cannot be retained at the mucosal surface for a long enough period to provide sustained release.

The compositions described in Dunn are completely different from the compositions of the invention and Dunn does not provide any teaching that would have helped the skilled person prepare a composition as claimed in the present application.

Moreover, the disclosures of Chenite and Dunn are so unrelated to each other that one skilled in the art would not consider them in any way combinable, especially in the absence of the hindsight of the present application. Even if these references were to be combined, the combination does not disclose all of the components of the claimed invention.

Reconsideration and withdrawal of the obviousness rejection are respectfully requested.

An additional Information Disclosure Statement is being submitted separately but along with this Amendment. Consideration of the information submitted and acknowledgement of such consideration are respectfully requested.

Moreover, reconsideration and withdrawal of the restriction requirement and the rejoinder of the provisionally non-elected claims, and an early Notice of Allowance with respect to all claims are respectfully requested.

Respectfully submitted,

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June 8, 2010 By: _____
(Date)

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